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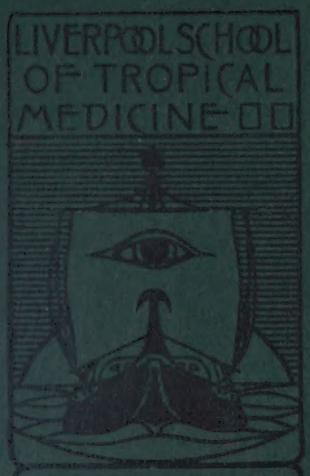

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SOME ENUMERATIVE STUDIES ON MALARIAL FEVER

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SOME ENUMERATIVE STUDIES ON MALARIAL FEVER

BY

MAJOR RONALD ROSS, F.R.S.,

AND

DAVID THOMSON, M.B., CH.B., D.P.H.

(*Received for publication* 15 *November*, 1910)*

1. *Preliminary.* For many years past little information which is both new and exact has been added to our knowledge of the pathology of malaria. This has probably been due to the exhaustion of the older methods of research which, being purely qualitative, have failed to indicate the precise correlations between the numbers of the parasites present in a patient and the various pathological and therapeutical reactions. For example, out of fifty-one and thirty-eight successful inoculations of men by means of infected blood and infected Anophelines respectively, in not a single one has any exact estimate been given of the number of parasites inoculated or recovered after the lapse of the incubation period; and, though many researches on quinine have been made, we know of none in which its direct effect upon the numbers of the parasites in the patient has been correctly measured. Moreover, the older methods often failed to reveal the parasites at all, unless they were present in large numbers. Hence our first care was to elaborate more exact methods both for detection and for enumeration. This was done early in the year (by R.R. and D.T.), though we have by no means reached finality yet. The new methods were next employed for all the cases in the Tropical Ward, daily counts of the parasites and often of the leucocytes, together with other estimations, being made (by D.T.). At the same time parallel chemical studies were carried out and therapeutical ones, and the measurements were carefully charted and compared. Even at this preliminary stage the results (which are given at the end of this paper) include more accurate verifications of some old conjectures, and demonstrations of some new theorems.

* (Read before the Royal Society, Dec. 8th, and reprinted from Proc. Roy. Soc., Series B., Vol. LXXXIII, p. 159, with Addenda.)

2. *The detective method used.* In the ordinary methods the blood is spread out in a thin film, liquid or dry, one cubic millimetre covering say four square centimetres of area. If the field of the oil-immersion lens has a diameter of 0·165 mm. and can be thoroughly searched by the eye in three seconds, about twelve hours' work would be required to examine the whole of 1 c.mm. of blood in this way; and if the specimen contains only one parasite it may not, by bad luck, be found until nearly the whole of the area has been searched. We have therefore employed the 'thick film process' described by one of us (R.R.) in 1903. In this 1 c.mm. of blood is spread out over only about one-quarter of a square centimetre or less, and dried; the haemoglobin is then gently washed out with water; and the residue, consisting of parasites, leucocytes, platelets, and the stromata of the red corpuscles, is carefully stained by any convenient method, with or without fixation. By this simple means the whole of a cubic millimetre of blood can be searched in less than an hour; but the identification of the Plasmodia requires considerable practice.

3. *The enumerative method used.* The younger *Plasmodia* are too small to be counted by the use of an ordinary haemocytometer; hence their number has usually been estimated by comparison with the number of red or white cells, the latter figure being determined by the haemocytometer. This gives a large compound error; for if e is the percentage error made in counting the red or white cells in one specimen, and e^1 is the percentage error made in computing the proportion of parasites to each corpuscle in that specimen, then, by a simple calculation, the total percentage error will be $e + e^1 + ee^1/100$. (For example, if $e = +5\%$ and $e^1 = +10\%$, the total percentage error will be $+15{\cdot}5\%$.)

Our method consists simply in making a measured quantity of blood into a thick film preparation and then counting *all* the parasites in it. The blood is measured by determining the diameter of a fine capillary tube under the microscope, and then calculating and marking off the length of the tube required to hold a given quantity (as suggested by Dr. Wakelin Barratt). Thus a uniform tube of 0·180 mm. diameter and 4 cm. length will contain 1·018 c.mm.—a convenient size. The blood is sucked into the tube

and then quickly discharged upon the glass-slide in one or several measured droplets, first samples being rejected. The dehaemoglobinized thick film is fixed before staining in order to avoid loss, and the whole area is scrupulously searched with the aid of a sliding stage.

Mr. M. Greenwood, Junr., informs me that if n is the number of parasites counted in the unit (say 1 c.mm.) of blood, and m is the number of such units in the patient's whole body, then the total number of parasites in him, assuming uniform distribution, will be $mn \pm 0{\cdot}67449m\sqrt{n}$. Thus the probable percentage error is $67{\cdot}449/\sqrt{n}$, the factor m cancelling out from the ratio. This is important, because it shows that the error depends, not on the magnitude of the measured sample taken, but upon the number of parasites actually counted in it. Hence, in order to obtain results within an assigned error, we take a large sample when the parasites are scarce and a small one when they are numerous; the number of parasites which we must find and count being given by the formula $n = 4550/e^2$, where e is the permissible error.

The greatest error occurs when the parasites are so scarce that it is difficult to find enough of them to count up to the required standard; or when they are so numerous that it is difficult to measure a volume of blood small enough to contain an easily countable number of them. In these preliminary researches we have seldom examined at one sitting more than 1 c.mm. of blood, or less than $\frac{1}{4}$ c.mm.

When the parasites were very numerous we have sometimes fallen back on estimating their number by comparison with leucocytes, but are now elaborating improvements and special instruments for such, and other, details. The method is also accurate and rapid for other blood parasites, and for leucocytes. Other sources of error are (1) inaccurate measurements of the quantity of blood used, and (2) difficulty of seeing or distinguishing badly stained parasites.

One kilogram of blood of average density (1057·5) contains 945,626 cubic millimetres, and the blood in a man's body is estimated to weigh about 4·9 per cent. of the total body weight, from which data it is easy to compute the total number of parasites in a patient. A man of 64·74 kilograms, or about ten stone, will contain about 3,000,000 c.mm. of blood.

4. *The cases studied* by us numbered thirty-three. All had been infected in West Africa or America, so that none was of less than some weeks' duration when admitted into hospital in Liverpool. All were males of from eighteen to sixty years of age. They were mostly shipmen or traders, and two were negroes. The parasites of all were counted almost every day, and sometimes several times a day; and the temperatures were taken every four hours, or more often. One case showed *Plasmodium malariae*, together with crescents (sexual forms of *P. falciparum*). Eight showed *P. vivax* only, and twenty-four *P. falciparum* only, two of the latter containing only sexual forms. Quinine was often withheld for some days while other methods of treatment were used. The cases were studied for 600 days altogether. There were no deaths.

All the cases are tabulated at the end of the paper for verification of details, and charts of cases 17 and 20 are given. At this preliminary stage of the enquiry we have undertaken to study only the gross daily correlations between the numbers of parasites and other phenomena, leaving more minute hourly and four-hourly analysis to future work. Hence if a number of counts or other observations have been made on one day we have recorded only the averages in the tables. For temperatures, however, it has been thought best to record maxima instead of averages, and, as the tables should be as economical as possible, we have used the *haemato thermic scale* suggested by one of us (R.R.), in which the ten degrees between 95° and 105° F., or between 35° and 45° C., are divided into 100 parts. Except Case 6, specially studied by Dr. Fantham, we have not distinguished in the tables the various forms, sets or stages of *P. vivax*, this being reserved for future study. Similarly, the treatment, leucocytes, haemoglobin and urobilin are not differentiated too minutely. Case 25 was counted by Dr. Korke.

5. *The correlation between the parasites and the fever.* It is well known that fever is caused only by the asexual forms of the parasites; but though these are generally thought to be more abundant during pyrexial periods, no extensive numerical studies on the point appear to have been made, with the result that some sceptics still profess doubts on the subject. Our cases, except four without fever (Cases 1, 15, 16, 27), would seem to

indicate a very strong, almost convincing, correlation. Twenty-one of them suffered each from one pyrexial period, lasting from one to seven days and preceded or followed by apyrexia; and in all except Case 32, the asexual parasites were very much more numerous during the pyrexial period. Nine of the cases (7, 17, 18, 19, 20, 23, 24, 26, 32) suffered from one or two relapses each (thirteen relapses altogether); and every relapse, as well as every original attack, was associated with a comparatively large number of parasites (forty-three pyrexial periods altogether). Similarly, there were forty-six apyrexial periods (including the four cases without fever), all associated with comparatively small numbers of asexual parasites; and conversely not a single marked rise in the number of asexual parasites took place without corresponding fever.

For further details we compare the numbers of parasites per c.mm. counted on days of fever with those counted on days without fever. A febrile day is taken as any one on which the patients' temperature exceeds 98·6° F. (=36° Haematothermic Scale), or any one which comes between two tertian paroxysms (Cases 9, 14, 24). The non-febrile days on which no asexual forms could be found in 1 c.mm. of blood are omitted. The results are:—

	Cases	Days	Total parasites	Average per day	Ratio
P. vivax—					
Fever	8	30	136,062	4,535	36·3
No fever	8	68	8,487	125	—
P. falciparum—					
Fever	21	97	1,319,880	13,607	29·6
No fever	19	83	38,277	461	—

If we had not omitted the non-febrile days on which no parasites were found, the non-febrile daily averages would have been much smaller than the figures given above, and the ratio of the febrile averages to them much larger; so that the febrile excess is very marked. An examination of the details will further convince the reader of the great fall in temperature which accompanies the fall

in the number of parasites. We should note that the comparatively small numbers of *P. vivax* found are due to the fact that the specimens generally contained a large proportion of mature parasites, not as yet disintegrated into spores—these, of course, being absent from peripheral blood containing *P. falciparum*, in which only spores or young forms generally occur. There is no reason for considering quinine in this connection, because it probably affects the fever only through its action on the parasites.

6. *The degree of fever associated with various numbers of parasites.* We know of no extensive and exact studies on this point, and ours are not yet complete. On forty-seven occasions the number of parasites was carefully compared with the maximum degree of temperature reached during the febrile paroxysm caused by them, and the following results were obtained:—

P. vivax (12 occasions)—					
No. of parasites	1,500	1,400	580	440	430
Maximum temp. °H.F. * ...	84	101	97	102	76
No. of parasites	260	256	232	150	133
Maximum temp. H.F.	76	54	46	44	34
No. of parasites	100	83			
Maximum temp. H.F.	34	20 (rigor)			
Co-efficient of correlation r		= 0·68561	± 0·10318		
P. falciparum (35 occasions)—					
No. of parasites	303,000	58,000	55,000	54,000	50,000
Maximum temp. °H.F.	108	82	88	100	98
No. of parasites	45,000	36,000	34,000	31,000	26,000
Maximum temp. H.F.	76	60	86	76	94
No. of parasites	26,000	25,000	16,000	15,000	15,000
Maximum temp. H.F.	101	80	52	54	54
No. of parasites	15,000	9,700	9,000	7,500	7,400
Maximum temp. H.F.	70	56	70	90	40
No. of parasites	6,700	6,500	6,000	5,800	5,200
Maximum temp. H.F.	86	83	52	70	76
No. of parasites	4,000	4,000	3,600	3,000	2,600
Maximum temp. H.F.	70	40	80	38	64
No. of parasites	2,500	2,000	1,860	1,000	200
Maximum temp. H.F.	50	46	38	15	50
Co-efficient of correlation r		= 0·60331	± 0·0·7251		

* H.F. = Haematothermic scale Fahrenheit.

These figures, together with the numerous ones given in the table of cases, show a very marked correlation, but there are, of course, many minor deviations. In numbers of the specimens there were certainly two sets of parasites of different ages, which were often counted together, though only one set could have been concerned with the fever. It is probable also, though by no means certain, that the resistance to the toxin of the *Plasmodia* varies, not only in different persons, but in the same person at different stages in the course of his infection and under different physiological conditions. Our new methods will, we hope, enable us shortly to undertake very detailed studies on these points.

7. *The pyrogenic limit.* It is quite evident that if the parasites fall below a certain limit they are no longer numerous enough to cause fever. Thus with *P. vivax*, an average of 125 parasites of all ages and forms counted during sixty-eight days in eight cases, and with *P. falciparum* an average of 460 asexual forms counted during eighty-three day in nineteen cases, failed to produce fever. The actual limit above which they become pyrogenic probably varies in different cases. With *P. vivax* as many as 1,500, 852 and 540 were found in Cases 2, 6, and 7 without fever, and as few as 150 and 50 in Cases 5 and 9 with very slight fever (98·6° F.), so that about 200 to 500 may perhaps be taken as the usual limit. With *P. falciparum*, as many as 1,620 (asexual) were found as an average of four non-febrile days in Case 26, and 1,196 as an average of six non-febrile days in Case 25; while in Case 18, from 16 to 1,860 were present for twenty-two days without causing any marked fever, so that 600 to 1,500 may perhaps be adopted as the usual limit. With *P. malariae* (Case 1), an average of 79 were present for thirteen days without fever, but about 140 twice caused slight rigor.

8. *The asexual forms between the relapses.* It is generally thought and taught that these forms tend to 'disappear' between the relapses—though of course exceptions, especially in children, are noted—and to reappear during them; and several hypotheses, such as that of parthenogenesis (F. Schaudinn) have been advanced explain the supposed phenomenon and have led to what appears to be much waste of work. We find that the asexual forms do not

necessarily disappear at all between the relapses, but are generally still to be found in small numbers per c.mm. on most of the days. The apyretic periods preceding the thirteen relapses in our cases (7, 17, 18, 19, 20, 23, 24, 26, 32) lasted 114 days altogether (nearly nine days each on the average). On eighteen of these days no observations were made; but on the remaining ninety-six days the parasites were found in small numbers in 59, or 61 per cent., and were not found only in 37. Moreover, the general trend of the curves suggests that they were not found on these days only because their numbers were a little too few for detection. The parasite curve, at its height during a pyrexial period, generally falls very rapidly at first and more slowly later, and tends to reach its lowest about half way between two apyrexial periods. At this point it may or may not remain above the detectable limit (by thick film methods). After this it was observed (by D.T.), especially in Cases 7, 17, 23 and 24, to begin mounting slowly at first, until when it reached the pyrogenic limit, another pyrexial period commenced. All this is scarcely compatible with the speculation that the apyrexial periods are due to the abrupt death of most of the asexual *Plasmodia*, or to their conversion into 'resting stages,' etc. Nor do such speculations appear to be at all necessary. It is easy to see that the survival of comparatively small numbers of the asexual forms will suffice to keep the infection alive, not only for the short periods observed by us, but for 'relapses of long interval,' and for months or years. Obviously, if only a few parasites per c.mm. are present, they may easily be overlooked in the small amount of blood (say 0·1 c.mm.) usually examined by thin film, and may then be reported as being absent: yet many millions may still exist in a patient who contains say 3,000,000 c.mm. of blood. The speculation regarding parthenogenesis in malaria and the case of Schaudinn, supposed to support it, have been criticised elsewhere by one of us (R.R.).* In two of our relapsing cases (19, 26) no sexual forms at all were found during thirty-five different thick film examinations. Even if they were present in small numbers (crescents do not collect in the spleen), yet the numbers of asexual parasites found in or just before the relapses (24 and 400 per c.mm.) cannot be explained by parthenogenesis unless we suppose that each

* Prevention of Malaria (Murray, 1910).

sexual form produced by 'gametoschizogony' 840 or 14,000 spores. Until better evidence for such views is adduced, our results justify the doctrine that the malarial infection is kept continuously alive simply by the persistence of the asexual form in varying numbers; and that fever occurs only when the forms are numerous enough to produce it.

9. *The effect of quinine on the asexual forms.* The destructive effect of the drug is of course everywhere recognised, though very little completely satisfactory statistical evidence can be cited in proof. Many laborious researches have been made regarding the comparative utility of the various salts, but these have been confined almost entirely to estimating the rate and percentage of absorption, judged from urinary elimination. The subject is of the greatest sanitary and medical importance; but, so far as we can see, it can be usefully studied only by the more detailed enumerative analysis which we propose soon to undertake. Our daily analysis gives little more light; but the following figures may be mentioned. Cases 15, 16 showed no asexual forms; Cases 11 and 13 were so severe that quinine was given at once; Cases 1, 5, 27, 31 and 32 were so mild that quinine was withheld during the period of observation; and in the remaining cases the drug was withheld only for some days (except an occasional necessary dose) and was then given continuously while the parasites were being counted. We have therefore added together all the daily counts during the periods of no-quinine and quinine respectively. With eight cases of *P. vivax* there were forty-five no-quinine days showing 104,032 total parasites, or an average of 2,312 a day; and there were 74 quinine days with 31,769 total parasites, or an average of only 429 a day (one-fifth). With *P. falciparum* (19 cases), 147 no-quinine days showed an average of 31,136 asexual forms, and 148 quinine days an average of 1,535 (one-half). We should have expected that the proportion of quinine-day parasites would have been smaller; but the no-quinine counts are diminished by the inclusion of the five mild cases and also by doses of 10 to 20 grains which were given on ten isolated occasions. On quinine days the doses are generally 20 to 30 grains a day, and Cases 11, 13, 14, 15 and 16 and parts of other cases are omitted because they were unsuitable. Great falls in the number of parasites occurred, even

without quinine, in Cases 5, 17 and 26; while, on the other hand, small numbers of asexual forms remained in some cases for five or more days in spite of considerable daily dosage. In Case 23 a severe relapse began six days after the stoppage of quinine tannate, which had been given for nine previous days in ten to thirty grain doses daily. No other relapses occurred after continuous quinine treatment; but twelve occurred without it.

10. *Observations on the sexual forms.* It is, of course, generally held—and probably quite rightly—that these are developed (by a cytological process not yet clearly seen) from the asexual forms. But at the same time no one has been able to note any correspondence between their numbers—many of the former may be present when the latter are very scarce, and vice versa. This rule, which is fully confirmed by our figures, has always been difficult to reconcile with the accepted theory of origin. On comparing our curves, however, the remarkable fact was observed (by D. T.) that there often seems to be indeed a correspondence, but that it is delayed for from eight to ten days—that is, that the sexual curve tends to rise that number of days after a rise in the asexual curve. Out of our twenty-five infections with *P. falciparum* eighteen showed crescents, and of these cases, 14, 22, 17, 18, 20, 23, 24 and 30 suggest this phenomenon, while in 17 and 20 the rises are sufficiently isolated to show it most distinctly. In Case 17, asexual rises existed on the 1st-3rd days, the 11th-12th and the 21st-22nd days, separated by apyrexial periods during which few asexual and no sexual forms were found; but on the 30th day (eight days after the last relapse) crescents appeared for the first time. In Case 20 an asexual relapse commenced on the 17th day and reached its height on the 20th day. A very few crescents had been found all the time; but a marked rise in their numbers commenced on the 26th day and reached its height on the 28th day. The most ready explanation is that the *crescents require eight to ten days for development*, during which they remain undetected, probably in the internal organs of the host. This is confirmed by the fact that numerous small ones are seen at the commencement of a rise; and also by the observation (frequently made) that in fresh infections the crescents seldom appear until a

week or more after the first attack of fever. Strong confirmation is also given by Case 6, in which Dr. Fantham noted a sudden appearance of sexual forms (*P. vivax*) on the 11th day, seven to ten days after the original asexual rise and after the patient had been taking thirty grains of quinine daily for a week—suggesting that the same phenomenon holds for *P. vivax* also.

Other observations are as follows:—(1) By no means every asexual rise is followed by a sexual one. In seven cases (13, 19, 25, 26, 28, 31, 33) no crescents at all were seen. In Case 13, a negro, 173,400 asexual forms per c.mm. failed to produce any; and none was observed in another negro (Case 28). (2) The number of crescents never exceeded five per cent. of asexual forms found in the generation which (hypothetically) produced them, and were generally in much smaller proportion. (3) We could find no relation to youth, vigour, amount of haemoglobin, duration of infection (from three to thirty weeks), or season of first infection. (4) The daily counts of crescents generally show marked daily variations, but we think that after considerable doses of quinine have been given for some days these daily variations tend to be smoothed out (Cases 16, 18, 22, 24). (5) In Cases 15, 14 and 16, particularly, a distinct tertian tendency was observed in the daily variations of crescents. This appears not to have been previously noticed, but is just what would be expected in the case of a tertian parasite—though, of course, the curve would be confused in a double tertian. (6) Sometimes the crescent curve suddenly rises with great rapidity, reaches its maximum, and then begins to fall on the next day with equal rapidity, though, later, the fall often tends to be much more slow (Cases 14, 15, 22, 23), especially when the numbers are very small. Apparently, the greater the maximum the quicker fall (Cases 14, 15); and the fall is sometimes jagged with a tertian tendency (ibid.). (7) Sometimes the maximum is irregularly maintained for a number of days (Cases 16, 18, 24), especially when quinine has not been previously given. (8) The crescents remained detectable for as many as 31, 32, 32, 35 and 44 days in Cases 20, 22, 23, 24 and 18 respectively; and finally disappeared (in 1 c.mm. of blood) in Cases 1, 11, 12, 16, 21 and 23.

From these data we think (1) that a varying percentage of asexual forms (sometimes very few or none) are constantly

generating crescents, which, after about eight to ten days, appear in the peripheral blood. Hence, when the asexual forms remain sufficiently numerous for a period, as when no quinine is given, the stock of crescents is being constantly replenished. Thus the mortality among the older crescents is constantly being compensated for by new arrivals, and the total numbers appear to remain constant—an appearance which has given rise to the generally accepted hypothesis (perhaps erroneous) that the crescents survive for weeks. On the other hand the sudden rise and fall of their numbers seen in Cases 14, 15, 22 and 23, suggest that they really survive only for a short time after their appearance in the peripheral blood. In Cases 16 and 24, however, a few crescents were still found after quinine had been given continuously for sixteen to eighteen days, suggesting that some of them may be able to survive for longer periods. In Cases 20, 22 and 23, they appeared in increasing numbers for four to six days after continuous 30-grain doses of quinine had been commenced, suggesting that the drug has no effect upon them when they have once been generated. But quinine appears to affect the numbers of crescents indirectly by cutting off the source of supply. Though many researches upon the effect of quinine on crescents (a subject of the greatest sanitary importance) have been attempted, so far as we know the possibility of a constantly continued supply has not previously been taken into consideration. We are continuing researches on the point.

11. *The leucocytes* were counted frequently, but not always daily; at first by the haemocytometer, but in the later twenty cases by the thick film method. The latter method has the advantages of putting the leucocytes closer together and of enabling us to estimate them at the same time with the parasites; but, like the haemocytometer, it is not very appropriate for differential counts because of occasional uncertainty in distinguishing the various kinds. Accordingly these were made (in six cases) by thin films, 500 cells being examined on each occasion.

Our results are, as shown in all the cases, that during the pyrexial periods the total leucocytes are comparatively few, being frequently as low as 2 to 3,000 per c.mm. (Cases 17, 18, 23, 24, etc.). But as

the asexual forms and the fever diminish the total leucocyte curve rises, and about seven days later exceeds the normal and may reach 20,000 and even, rarely, 30,000 per c.mm. (Case 7)—though this height is not maintained. The very high counts seem to be associated with much quinine. We observed generally that the so-called polymorphonuclear leucocytes, though rather few during the pyrexial periods, do not vary much from day to day, but about seven days after the fever has abated their numbers are markedly increased and vary much. The so-called mononuclear percentage was, however, always in excess throughout the cases, even long after disappearance of all forms of the parasites—for six weeks afterwards in Case 1, though quinine had been given daily during that period (out of hospital). We think, therefore, that a high mononuclear percentage is likely to be always of value in diagnosis in the absence of parasites. The normal ratio of all mononuclears to polymorphonuclears is about 35 per cent., but in our cases it was often 60 per cent., and in Case 30 reached 80 per cent. It tends to fall slightly with great improvement in health. Thus the total leucocyte rise appears to be due chiefly to mononuclears. During the individual daily paroxysms, as shown by Stephens and Christophers,* the total mononuclears are rather low during the height of the fever, but show a marked increase during the following remission, this increase affecting chiefly the large mononuclears. This process is repeated with each paroxysm, and if a paroxysm fails the mononuclears remain increased (Case 9 especially). But we could not always find these variations in the absence of fever and many parasites. This mononuclear reaction, which we have also seen in our case of trypanosomiasis, appears to be exactly comparable to the polymorphonuclear reaction described by F. W. Andrews ('Lancet,' June, July, 1910) as generally occurring in bacterial diseases.

12. *Various therapeutic agents.* Methylene blue was tried in three cases in 12 grain daily doses; the parasites diminished, but we cannot draw any conclusions from the figures. In Case 24, altogether 36 grains of soamin were injected intramuscularly in

* The increase in the number of large mononuclear leucocytes as a diagnostic sign of malaria. Royal Society's Malaria Committee Reports, Fifth Series, 1901. Harrison & Sons, London.

5 to 10 grain doses on five occasions during twelve days, and yet a smart relapse occurred during and after the last dose. In the same case just before the same relapse X-rays had been applied over the spleen and abdomen for twenty minutes. The asexual parasite rise had commenced before the application. In Case 24, faradic and galvanic currents were applied over the spleen, each for ten minutes, but crescent counts made immediately before and two hours after the application remained unaltered.

13. *Haemoglobin.* This was estimated in most of the later cases. The percentage always fell during fever and began to rise rapidly shortly afterwards, proving the destructive effect of the parasites and the rapid recuperation of the patients. The greatest fall was 25 per cent. after four days' fever (Case 20); but more detailed work is required to trace correspondence with the number of parasites. The lowest percentage found was 53 per cent. All the patients were anaemic at first, but the haemoglobin rose rapidly with improvement of health, and very rapidly in the more vigorous subjects. We decided not to attempt counts of red corpuscles, as these have been made so frequently already. The elimination of the haemoglobin and the findings in a case of blackwater fever will be dealt with in the two following papers by Dr. Simpson and in one by ourselves.

14. *Summary.* (1) There would seem to be a very decided correlation between the number of asexual *Plasmodia* found in the peripheral blood and the fever.

(2) As a rule, no fever exists unless the asexual forms exceed some hundreds per c.mm.

(3) The asexual forms do not always disappear between relapses (as often thought) but tend to persist in small numbers per c.mm., and often increase again for some days before the actual febrile relapse occurs.

(4) These observations give a coherent theory of the malarial invasion, according to which the infection is kept alive indefinitely by the ordinary sporulation of the asexual forms, and not by parthenogenesis or by resistant forms; and fever recurs only when the parasites are numerous enough to produce it.

(5) We estimate from our cases that considerable continued doses of quinine reduced the asexual forms by 50 to 80 per cent.

(6) There are strong reasons for supposing that the sexual forms require eight to ten days for development; that the often noticed long persistence of crescents is not due to their long life (as generally thought) but to constant replenishments of the stock by fresh broods; that they sometimes show a distinct tertian periodicity; and that quinine does not affect them when once generated; but ultimately reduces their numbers by destroying the generating cells. The sexual forms were never seen to produce fever.

(7) The leucocytes are below normal during febrile periods and above normal afterwards. The percentage of mononuclears rises after paroxysms and is always in excess of the normal.

(8) Methylene blue, soamin, X-rays, and faradic and galvanic currents had no results in a few experiments.

(9) The haemoglobin falls markedly with fever, but rises rapidly with convalesence.

(10) The faecal urobilin shows marked correlation with the occurrence of fever, and is specially studied in the accompanying paper by Dr. G. C. E. Simpson.

Many other deductions may be based on our observations, but will be better considered after more detailed counts have been made.

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TABLE GIVING THE DAILY DETAILS OF 33 CASES OF MALARIA STUDIED BY ENUMERATIVE METHODS

NOTE.—The headline of each case gives initials, calling, age, where infected (presumably), how long previously infected (presumably), month of admission, and body weight on admission. The maximum temperatures are given in the Haematothermic Fahrenheit scale (H.F.), which equals the excess over 95°F., multiplied by 10. The leucocytes are recorded in hundreds per c.mm.; the haemoglobin either in the Talqvist or the Sahli scale; the urobilin (either urinary or faecal) in milligrams; the drugs in grains; and the parasites (either all forms together or asexual and sexual forms separately) in numbers per c.mm.

A. *P. malariae* and *P. falciparum* (crescents only).

Case 1.—W. M., ship butcher, 42; West Africa; 70 days; February, 145 lbs.

Days	1	2	3	4	5	6	7
Total parasites	—	254	76	—	148	121	151
Crescents	200	164	170	—	180	141	156
Maximum temp.	26	20 (rigor)	20	22	30	34 (rigor)	30
Methylene blue, grs.	—	—	—	—	4	12	12
Polychr. methylene blue, c.c.	—	—	—	—	—	—	—
Ur. urob., mgr.	20	?	18	0	0	—	—

Days	8	9	10	11	12	13	14
Total parasites	127	140	57	17	17	23	8
Crescents	220	117	86	70	51	38	16
Maximum temp.	40	30	30	30	16	22	34
Methylene blue, grs.	12	12	12	12	12	12	0
Polychr. methylene blue, c.c.	—	—	—	—	—	—	—
Ur. urob., mgr.	—	—	—	—	—	—	—

Days	15	16	17	18	19	20	21
Total parasites	16	6	0	—	0	0	0
Crescents	10	10	0	—	2	2	2
Maximum temp.	34	30	34	24	30	30	22
Methylene blue, grs.	—	—	—	—	4	12	12
Polychr. methylene blue, c.c.	15	45	30	0	—	—	—
Ur. urob., mgr.	—	—	—	—	—	—	—

B. *P. vivax.*

Case 2.—J. B., seaman, 26; Colon; 120 days; January, 147 lbs.

Days	1	2	3	4	5	6	7
Total parasites	8,766	6,233	2,630	1,500	1,260	—	0
Maximum temp.	48	38	58	20	24	24	18
Q. hydrochloride, grs.	0	15	30	30	30	30	30

Case 3.—J. H., seaman, 50; W. Africa; 35 days; January, ?

Days	1	2	3	4	5	6	to 11
Total parasites	11,019	1,444	642	88	40	0	0
Maximum temp.	84	42	44	34	32	22	normal
Q. sulph., grs.	—	—	—	—	20	20	20
Ur. urob., mgs.	2	0	0	0	0	—	—

Case 4.—J. Hough, ship steward, 22; Vera Cruz; 112 days; March, 105 lbs.

Days	1	2	3	4	5	6	7
Total parasites	370	308	505	280	46	8	0
Maximum temp.	46	44	76	58	30	26	28
Q. hydrochloride, grs.	—	—	—	30	30	30	30
Total leucocytes	—	55	—	86	—	—	—
Hb. Tal., percentage	90	85	85	80	85	85	85
Ur. urob., mgs.	54	0	18	82	140	17	19
Days	8	9	11	—	—	—	—
Total parasites	0	0	0	—	—	—	—
Maximum temp.	20	24	14	—	—	—	—
Q. hydrochloride, grs.	30	30	30	—	—	—	—
Total leucocytes	84	—	160	—	—	—	—
Hb. Tal., percentage	85	85	90	—	—	—	—
Ur. urob., mgs.	0	0	—	—	—	—	—

Case 5.—R. R., planter, 25; Fernando Po; 75 days; March, 129 lbs.

Days	1	2	3	4	5	6	7
Total parasites	28,700	7,753	1,153	1,000	150	200	140
Maximum temp.	92	60	76	50	36	36	26
Methylene blue, grs.	—	—	—	12	12	12	12
Total leucocytes	—	65	50	56	71	47	48
Hb. Tal., percentage	—	90	85	80	85	85	80
Ur. urob., mgs.	19	14	23	12	—	—	—
Faec. urob., mgs.	0	27	0	0	—	—	—

Case 5—continued

Days	8	9	10	11	12	13	14
Total parasites	200	64	96	32	78	0	26
Maximum temp.	20	28	32	24	18	16	26
Methylene blue, grs.	12	12	12	12	—	—	—
Total leucocytes	—	43	—	—	—	—	—
Hb. Tal., percentage	90	90	90	90	90	90	90
Ur. urob., mgs.	—	—	—	—	—	—	—
Faec. urob., mgs.	—	—	—	—	—	—	—
Days	15	16	—	—	—	—	—
Total parasites	6	30	—	—	—	—	—
Maximum temp.	28	22	—	—	—	—	—
Methylene blue, grs.	—	—	—	—	—	—	—
Total leucocytes	78	—	—	—	—	—	—
Hb. Tal., percentage	90	90	—	—	—	—	—
Ur. urob., mgs.	—	—	—	—	—	—	—
Faec. urob., mgs.	—	—	—	—	—	—	—

Case 6.—J. M., sailor, 19; Niger; 135 days; April, ?

Days	1	2	3	4	5	6	7
As. parasites	852	668	1,080	256	64	68	44
Sex. parasites	—	—	—	—	—	—	—
Maximum temp.	26	70	102	82	20	24	20
Q. bihydrochloride, grs. ...	0	0	0	30	30	30	30
Ur. urob., mgs.	—	18	1	115	15	0	15
Faec. urob., mgs.	—	—	—	286	403	130	83
Days	8	9	10	11	12	13	14
As. parasites	24	8	28	—	—	—	—
Sex. parasites	—	—	—	412	144	56	16
Maximum temp.	24	16	20	14	20	26	22
Q. bihydrochloride, grs. ...	30	30	30	30	30	30	30
Ur. urob., mgs.	0	0	—	—	—	—	?
Faec. urob., mgs.	100	—	—	—	—	—	20

Case 6—continued

Days	15	16	17	18	—	—	—
As. parasites	—	—	—	—	—	—	—
Sex. parasites	48	52	20	8	—	—	—
Maximum temp.	24	10	24	34	—	—	—
Q. bihydrochloride, grs. ...	30	30	30	30	—	—	—
Ur. urob., mgs.	—	—	—	—	—	—	—
Faec. urob., mgs.	—	—	—	—	—	—	—

Case 7.—W. M., fireman, 35; Niger; 90 days; May, 155 lbs.

Days	1	2	3	4	5	6	7
Total parasites	—	440	1,300	133	250	152	148
Maximum temp.	22	102	66	34	30	28	26
Q. hydrochloride, grs.	0	10	0	0	0	0	0
Total leucocytes	20	40	22	85	110	56	150
Hb. Tal., percentage	70	80	75	85	90	85	80
Faec. urob., mgs.	—	0	530	340	88	0	200

Days	8	9	10	11	12	13	14
Total parasites	28	96	100	130	80	124	228
Maximum temp.	26	24	34	24	26	30	28
Q. hydrochloride, grs.	0	0	0	0	0	0	0
Total leucocytes	215	151	59	62	230	149	110
Hb. Tal., percentage	85	85	—	80	90	90	—
Faec. urob., mgs.	130	0	0	0	70	50	—

Days	15	16	17	18	19	20	21
Total parasites	284	368	540	280	400	440	50
Maximum temp.	42	54	22	30	20	32	20
Q. hydrochloride, grs.	0	10	30	30	30	30	30
Total leucocytes	61	100	70	80	24	71	45
Hb. Tal., percentage	80	80	80	85	Sahli per cent.	80	80
Faec. urob., mgs.	—	—	—	—	—	—	—

C. *P. falciparum*—

Case 10.—A. M. ship engineer, 37; Kamerun, 140 days; January, 145 lbs.

Days	1	2	3	4	5	6	7
*As. parasites	1,000	10,000	14,700	8,650	2,600	0	—
Crescents	—	—	—	—	—	137	73
Maximum temp.	62	58	38	54	26	20	18
Q. sulph., grs.	—	—	—	20	20	20	20
Ur. urob., mgs.	—	100	75	75	155	45	20
Days	8	—	—	—	—	—	—
As. parasites	—	—	—	—	—	—	—
Crescents	13	—	—	—	—	—	—
Maximum temp.	18	—	—	—	—	—	—
Q. sulph., grs.	20	—	—	—	—	—	—
Ur. urob., mgs.	17	—	—	—	—	—	—

Case 11.—W. M., steward, 17; Niger; 190 days; January, 126 lbs.

Days	1	2	3	4	5	6	7
As. parasites	56,257	55,300	0	0	0	0	0
Crescents	—	—	4	16	0	15	0
Maximum temp.	90	68	44	18	20	16	17
Q. hydrochloride, grs.	30	30	30	30	30	30	30
Ur. urob., mgs.	75	1,730	500	250	237	120	9
Days	8	9	10	11	12	13	14
As. parasites	—	—	—	0	0	—	—
Crescents	(*et seq.* 5 days)		—	—	—	—	—
Maximum temp.	30	24	34	24	20	24	34
Q. hydrochloride, grs.	15	15	15	15	15	15	15
Ur. urob., mgs.	55	0	0	50	20	0	0

Case 12.—C. H., seaman, 24; Niger, 30 days; January, 112 lbs.

Days	1	2	3	4	5	6	7
As. parasites	24,600	47,000	45,250	2,250	0	0	0
Crescents	—	—	—	—	180	168	—
Maximum temp.	50	86	64	42	32	20	18
Q. sulph., grs.	—	—	20	20	20	20	10
Ur. urob., mgs.	128	133	125	143	51	50	90

* As. = Asexual.

Case 12—*continued*

Days	8	9	10	11	12	13	14
As. parasites	0	0	0	0	0	0	0
Crescents	48	72	25	26	34	37	9
Maximum temp.	20	18	20	18	20	18	12
Q. sulph., grs.	10	10	10	10	10	10	10
Ur. urob., mgs.	0	0	40	18	0	27	17
Days	15	16	17	—	—	—	—
As. parasites	—	—	—	—	—	—	—
Crescents	8	—	5	—	—	—	—
Maximum temp.	22	12	12	—	—	—	—
Q. sulph., grs.	—	10	10	—	—	—	—
Ur. urob., mgs.	0	0	—	—	—	—	—

Case 13.—G. N., negro seaman, 22; Congo; 30 days; January, 118 lbs.

Days	1	2	3	4	5	6	7
As. parasites	181,933	173,400	60,100	673	0	0	0
Crescents	0	0	0	0	0	0	0
Maximum temp.	108	100	46	50	26	20	20
Q. hydrochloride	30	30	30	30	30	30	30
Ur. urob., mgs.	—	—	680	100	100	100	60
Days	8	9	—	—	—	—	—
As. parasites	0	0	—	—	—	—	—
Crescents	0	0	—	—	—	—	—
Maximum temp.	20	20	—	—	—	—	—
Q. hydrochloride	15	—	—	—	—	—	—
Ur. urob., mgs.	20	112	0 *et. seq.* (14 days)				

Case 14.—J. M., sailor, 31; Gold Coast; 56 days; January, 158 lbs.

Days	1	2	3	4	5	6	7
As. parasites	28,100	30,050	410	0	0	0	100
Crescents	—	—	—	565	1,190	2,000	1,200
Maximum temp.	76	30	44	14	20	16	18
Q. bihydrochloride, grs. ...	10	20	0	10	0	—	—
Total leucocytes	78	87	81	56	62	75	50
Ur. urob., mgs.	0	4	0	20	24	27	39

Case 14—*continued*

Days	8	9	10	11	12	13	14
As. parasites	0	0	0	0	0	0	0
Crescents	1,500	1,300	1,090	1,500	1,108	1,130	740
Maximum temp.	20	14	14	12	18	10	—
Q. bihydrochloride, grs. ...	—	—	—	—	—	—	—
Total leucocytes	56	81	80	56	59	62	62
Ur. urob., mgs.	39	11	9	—	—	—	—

Days	15	16	17	18	19	20	21
As. parasites	0	0	0	0	0	0	0
Crescents	1,022	691	336	422	—	162	95
Maximum temp.	—	—	—	—	—	—	—
Q. bihydrochloride, grs. ...	—	—	—	—	—	—	—
Total leucocytes	50	68	59	—	81	56	—
Ur. urob., mgs.	—	—	—	—	—	—	—

Case 15.—W. B., fireman, 27; Vera Cruz; 49 days; January, 126 lbs.

Days	1	2	3	4	5	6	7
As. parasites	0	—	—	—	—	—	—
Crescents	6,700	—	4,370	4,700	4,000	—	2,200
Maximum temp.	16	14	22	normal	—	—	—
Q. hydrochloride, grs.	30	30	30	30	15	*et seq.*	—
Total leucocytes	112	—	100	87	97	—	125
Ur. urob., mgs.	0	0	—	—	—	—	—

Days	8	9	10	11	12	—	—
As. parasites	—	—	—	—	—	—	—
Crescents	1,870	937	937	770	470	—	—
Maximum temp.	—	—	—	—	—	—	—
Q. hydrochloride, grs.	—	—	—	—	—	—	—
Total leucocytes	168	137	134	121	147	—	—
Ur. urob., mgs.	—	0	0	—	—	—	—

Case 16.—J. G., seaman, 17; W. Africa; 70 days; February, 126 lbs.

Days	1	2	3	4	5	6	7
As. parasites	0	—	—	—	—	—	—
Crescents	244	107	99	230	146	220	197
Maximum temp.	18	24	14 normal		—	—	—
Total leucocytes	75	81	93	112	122	137	115
Q. sulph., grs.	—	—	—	—	—	—	—

Days	8	9	10	11	12	13	14
As. parasites	—	—	—	—	—	—	—
Crescents	94	200	107	125	152	97	140
Maximum temp.	—	—	—	—	—	—	—
Total leucocytes	78	128	107	112	93	106	100
Q. sulph., grs.	—	—	—	20	20	10	10

Days	15	16	17	18	19	20	21
As. parasites	—	—	—	—	—	—	—
Crescents	86	60	47	65	44	51	32
Maximum temp.	—	—	—	—	—	—	—
Total leucocytes	122	100	93	131	134	137	—
Q. sulph., grs.	30	30	*et seq.*	—	—	—	—

Days	22	23	24	25	26	—	—
As. parasites	—	—	—	—	—	—	—
Crescents	8	10	20	10	6	—	—
Maximum temp.	—	—	—	—	—	—	—
Total leucocytes	—	—	—	—	—	—	—
Q. sulph., grs.	—	—	—	—	—	—	—

Case 17.—R. B., seaman, 19; Congo; 49 days; March, 134 lbs.

Days	1	2	3	4	5	6	7
As. parasites	5,250	380	2,837	336	288	184	60
Crescents	0	—	—	—	—	—	—
Maximum temp.	70	70	40	34	28	26	22
Q. hydrochloride	—	—	—	—	—	—	—
Total leucocytes	31	25	—	—	25	—	—
Hb. Tal., percentage	70	60	65	70	75	75	75
Ur. urob., mgs.	33	69	90	51	190	43	43
Faec. urob., mgs.	—	—	0	1,140	—	—	—

Case 17—continued

Days	8	9	10	11	12	13	14
As. parasites	36	55	12	1,750	360	0	8
Crescents	—	—	—	—	—	—	—
Maximum temp.	20	22	32	64	44	30	24
Q. hydrochloride	—	—	—	20	—	—	—
Total leucocytes	—	—	—	26	—	—	—
Hb. Tal., percentage	75	80	80	75	70	75	80
Ur. urob., mgs.	64	75	70	29	183	25	11
Faec. urob., mgs.	—	—	—	—	—	453	—

Days	15	16	17	18	19	20	21
As. parasites	0	12	0	0	28	60	1,325
Crescents	—	—	—	—	—	—	—
Maximum temp.	18	20	20	18	22	20	54
Q. hydrochloride	—	—	—	—	—	—	10
Total leucocytes	68	—	—	—	68	—	—
Hb. Tal., percentage	80	80	80	85	85	85	85
Ur. urob., mgs.	76	68	76	19	25	72	150
Faec. urob., mgs.	—	—	—	—	—	—	280

Days	22	23	24	25	26	27	28
As. parasites	1,250	0	8	0	0	0	0
Crescents	—	—	—	—	—	—	—
Maximum temp.	50	30	20	22	18	16	22
Q. hydrochloride	10	—	—	—	—	10	30
Total leucocytes	40	—	—	—	—	—	—
Hb. Tal., percentage	80	75	80	—	85	—	90
Ur. urob., mgs.	103	68	44	42	70	70	—
Faec. urob., mgs.	—	—	—	—	—	—	—

Case 17—*continued*

Days	29	30	31	32	33	34	35
As. parasites	0	0	—	—	—	—	—
Crescents	—	25	—	0	—	12	—
Maximum temp.	18	22	16	18	18	28	22
Q. hydrochloride	30	*et seq.*	—	—	—	—	—
Total leucocytes	125	—	—	—	—	—	—
Hb. Tal., percentage	—	90	—	85	—	90	—
Ur. urob., mgs.	—	45	0	—	—	—	—
Faec. urob., mgs.	—	—	—	—	—	—	—
Days	36	37	38	39	40	—	—
As. parasites	—	—	—	—	—	—	—
Crescents	0	—	—	12	—	—	—
Maximum temp.	26	30	28	26	24	—	—
Q. hydrochloride	—	—	—	—	—	—	—
Total leucocytes	—	—	—	—	—	—	—
Hb. Tal., percentage	90	—	90	—	90	—	—
Ur. urob., mgs.	—	—	—	—	—	—	—
Faec. urob., mgs.	—	—	—	—	—	—	—

Case 18.—A. C., steward, 29; Congo; 77 days; March, 100 lbs.

Days	1	2	3	4	5	6	7
As. parasites	32	—	0	—	24	—	128
Crescents	32	—	15	—	24	—	36
Maximum temp.	32	32	30	32	26	20	26
Q. hydrochloride	—	—	—	—	—	—	—
Ur. urob., mgs.	—	—	116	47	81	54	38
Days	8	9	10	11	12	13	14
As. parasites	—	26	—	80	64	—	388
Crescents	—	28	—	68	52	—	52
Maximum temp.	20	28	28	24	20	10	10
Q. hydrochloride	—	—	—	—	—	—	—
Ur. urob., mgs.	33	7	15	10	—	—	—

Case 18—*continued*

Days	15	16	17	18	19	20	21
As. parasites	—	1,860	20	744	60	0	0
Crescents	—	72	32	16	24	20	84
Maximum temp.	20	38	38	26	16	20	18
Q. hydrochloride	—	—	5	5	5	5	5
Ur. urob., mgs.	—	—	—	—	30	32	12
Days	22	23	24	25	26	27	28
As. parasites	16	0	0	0	0	0	0
Crescents	92	180	128	196	228	264	212
Maximum temp.	18	26	22	26	16	26	14
Q. hydrochloride	5	5	5	5	5	5	5
Ur. urob., mgs.	10	0	0	—	0	—	20
Days	29	30	31	32	33	34	35
As. parasites	0	30	32	0	0	—	—
Crescents	276	286	138	208	136	128	100
Maximum temp.	24	84	30	22	30	32	30
Q. hydrochloride	5	10	30	30	*et seq.*	—	—
Ur. urob., mgs.	0	0	—	—	—	—	—
Days	36	37	38	39	40	41	42
As. parasites	—	—	—	—	—	—	—
Crescents	50	50	+	48	—	16	—
Maximum temp.	20	42	22	24	—	—	—
Q. hydrochloride	—	—	—	—	—	—	—
Ur. urob., mgs.	—	—	—	—	—	—	—
Days	43	—	—	—	—	—	—
As. parasites	—	—	—	—	—	—	—
Crescents	8	—	—	—	—	—	—
Maximum temp.	—	—	—	—	—	—	—
Q. hydrochloride	—	—	—	—	—	—	—
Ur. urob., mgs.	—	—	—	—	—	—	—

Case 19.—H. R., sailor, 20; Niger; 40 days; March, 110 lbs.

Days	1	2	3	4	5	6	7
As. parasites	3,310	2,543	184	0	4	8	0
Crescents	None	—	—	—	—	—	—
Maximum temp.	76	75	32	32	22	16	20
Q. hydrochloride	—	20	—	—	—	—	—
Total leucocytes	37	31	—	—	—	51	—
Hb. Tal., percentage	60	50	65	70	70	75	80
Ur. urob., mgs.	67	0	132	144	170	115	39

Days	8	9	10	11	12	13	14
As. parasites	0	0	0	0	24	0	140
Crescents	—	—	—	—	—	—	—
Maximum temp.	28	24	24	32	24	42	32
Q. hydrochloride	—	—	—	—	—	—	—
Total leucocytes	—	—	—	94	—	—	—
Hb. Tal., percentage	80	80	85	85	80	80	85
Ur. urob., mgs.	108	116	38	40	42	0	38

Days	15	16	17	18	19	20	21
As. parasites	200	—	0	—	0	—	0
Crescents	—	—	—	—	—	—	—
Maximum temp.	54	36	26	20	20	22	18
Q. hydrochloride	10	30	30	*et seq.*	—	—	—
Total leucocytes	—	—	128	—	—	—	—
Hb. Tal., percentage	80	70	80	—	80	—	80
Ur. urob., mgs.	—	116	30	13	0	—	—

Case 20.—F. B., steward, 24; Niger; 40 days; March, 129 lbs.

Days	1	2	3	4	5	6	7
As. parasites	4,172	580	22	20	4	0	0
Crescents	0	0	0	0	0	4	12
Maximum temp.	90	56	70	40	24	22	20
Q. hydrochloride	10	0	20	—	—	—	—
Total leucocytes	—	—	—	37	—	—	60
Hb. Tal., percentage	60	55	60	75	75	80	75
Ur. urob., mgs.	0	273	182	162	81	54	29

Case 20—continued

Days	8	9	10	11	12	13	14
As. parasites	0	0	12	0	0	—	—
Crescents	8	16	12	—	0	—	—
Maximum temp.	26	28	24	24	26	20	26
Q. hydrochloride	—	—	—	—	—	—	—
Total leucocytes	—	—	100	—	—	—	—
Hb. Tal., percentage	80	80	80	—	85	80	—
Ur. urob., mgs.	32	40	26	0	0	70	70
Days	15	16	17	18	19	20	21
As. parasites	32	—	200	—	2,698	4,000	3,750
Crescents	0	—	4	—	0	0	4
Maximum temp.	22	22	26	46	74	70	76
Q. hydrochloride	—	—	—	—	—	10	30
Total leucocytes	150	—	—	—	90	46	—
Hb. Tal., percentage	85	—	80	—	83	83	S. per cent.
Ur. urob., mgs.	—	0	—	8	72	107	81
Days	22	23	24	25	26	27	28
As. parasites	1,560	104	0	—	0	—	320
Crescents	0	0	0	—	32	—	88
Maximum temp.	38	32	24	24	26	24	16
Q. hydrochloride	30	30	30	30	30	30	30
Total leucocytes	42	35	35	—	—	—	—
Hb. Tal., percentage	55	60	70	—	80	—	80
Ur. urob., mgs.	29	7	10	23	21	0	8
Days	29	30	31	32	33	34	35
As. parasites	—	0	—	0	—	0	—
Crescents	—	68	—	56	—	8	—
Maximum temp.	20	24	18	24	24	20	20
Q. hydrochloride	30	30	30	30	20	20	20
Total leucocytes	—	170	—	300	—	210	—
Hb. Tal., percentage	—	80	—	85	—	90	—
Ur. urob., mgs.	0	0	—	—	—	—	—

Case 20—*continued*

Days	36	37	—	—	—	—	—
As. parasites	—	0	—	—	—	—	—
Crescents	—	36	—	—	—	—	—
Maximum temp.	20	24	—	—	—	—	—
Q. hydrochloride	20	20	—	—	—	—	—
Total leucocytes	—	264	—	—	—	—	—
Hb. Tal., percentage	—	90	—	—	—	—	—
Ur. urob., mgs.	—	—	—	—	—	—	—

Case 21.—W. T., seaman, 50; Niger; 28 days; April, 158 lbs.

Days	1	2	3	4	5	6	7
As. parasites	36,000	25,300	16,000	280	0	0	300
Crescents	0	0	0	28	28	24	24
Maximum temp.	61	58	52	32	20	20	24
Q. bihydrochloride	—	—	20	30	30	30	—
Total leucocytes	—	25	—	43	—	—	—
Ur. urob. mgs.	—	10	48	1,300	273	54	40
Faec. urob., mgs.	—	—	0	0	30	4,100	?

Days	8	9	10	11	12	13	14
As. parasites	—	0	—	0	—	0	—
Crescents	—	16	—	4	—	8	—
Maximum temp.	24	34	26	26	22	26	24
Q. bihydrochloride	—	—	—	—	16	20	20
Total leucocytes	—	55	—	34	—	54	—
Ur. urob., mgs.	39	19	—	—	10	—	—
Faec. urob., mgs.	0	333	—	—	—	—	—

Days	15	16	17	18	19	20	—
As. parasites	—	—	0	—	—	0	—
Crescents	—	—	4	—	—	0	—
Maximum temp.	16	30	24	28	22	24	—
Q. bihydrochloride	20	20	10	10	10	10	—
Total leucocytes	—	—	75	—	—	119	—
Ur. urob., mgs.	—	—	—	—	—	—	—
Faec. urob., mgs.	—	—	—	—	153	—	—

Case 22.—C. G., sailor, 30; Niger; 40 days; April.

Days	1	2	3	4	5	6	7
As. parasites	7,920	—	20,250	44,800	920	30	50
Crescents	24	—	32	56	224	584	920
Maximum temp.	64	82	76	70	36	18	26
Q. bihydrochloride	—	10	30	30	30	30	30
Total leucocytes	—	—	—	130	200	80	50
Hb. Tal., percentage	—	85	80	82	80	80	86
Ur. urob., mgs.	0	0	1,500	0	50	70	34
Faec. urob., mgs.	1,730	780	0	1,670	0	?	116

Days	8	9	10	11	12	13	14
As. parasites	0	0	0	?	?	0	?
Crescents	1,128	1,180	1,384	1,288	1,240	948	892
Maximum temp.	24	24	18	26	14	24	18
Q. bihydrochloride	30	30	30	30	30	30	30
Total leucocytes	80	50	70	75	60	60	140
Hb. Tal., percentage	—	75	77	75	73	65	70
Ur. urob., mgs.	45	95	100	120	14	9	7
Faec. urob., mgs.	?	0	0	0	120	0	560

Days	15	16	17	18	19	20	21
As. parasites	0	0	0	0	0	—	—
Crescents	856	824	612	336	508	264	132
Maximum temp.	10	16	26	24	30	30	10
Q. bihydrochloride	30	30	30	10	10	20	—
Total leucocytes	100	78	60	180	90	140	92
Hb. Tal., percentage	75	80	85	—	85	—	85
Ur. urob., mgs.	23	38	18	0	12	0	0
Faec. urob., mgs.	220	386	113	0	?	0	—

Case 22—continued

Days	22	23	24	25	26	27	28
As. parasites	—	—	0	—	—	—	—
Crescents	190	120	100	40	32	—	20
Maximum temp.	10	16	14	22	20	10	10
Q. bihydrochloride	—	—	—	—	—	—	10
Total leucocytes	150	115	135	106	70	—	78
Hb. Tal., percentage	—	80	—	80	80	75	78
Ur. urob., mgs.	—	—	—	33	27	52	38
Faec. urob., mgs.	—	—	—	0	0	720	373

Days	29	30	31	32	33	34	—
As. parasites	—	—	—	—	—	—	—
Crescents	—	4	—	0	—	—	—
Maximum temp.	20	10	14	10	—	—	—
Q. bihydrochloride	10	10	10	10	—	—	—
Total leucocytes	—	100	—	160	—	—	—
Hb. Tal., percentage	84	85	82	82	—	—	—
Ur. urob., mgs.	10	0	—	—	—	—	—
Faec. urob., mgs.	0	0	?	0	0	10	—

Case. 23—T. C., sailor, 17; Niger; 21 days; April, 110 lbs.

Days	1	2	3	4	5	6	7
As. parasites	24,000	5,520	1,700	500	1,200	160	—
Crescents	—	—	—	—	—	160	—
Maximum temp.	98	90	32	30	28	14	14
Q. bihydrochloride	20	—	—	—	—	—	—
Total leucocytes	52	—	—	—	30	—	—
Hb. Tal., percentage	85	80	80	80	80	85	—

Days	8	9	10	11	12	13	14
As. parasites	28,500	22,600	1,600	340	0	0	0
Crescents	608	635	720	780	552	368	432
Maximum temp.	86	100	86	30	32	20	20
Q. bihydrochloride	tannate	10	20	30	30	30	30
Total leucocytes	—	48	—	—	40	52	—
Hb. Tal., percentage	75	75	75	73	65	70	—

Case 23—*continued*

Days	15	16	17	18	19	20	21
As. parasites	0	0	0	0	—	480	—
Crescents	500	464	468	468	—	344	—
Maximum temp.	28	20	32	20	30	28	24
Q. bihydrochloride	30	30	20	—	—	—	—
Total leucocytes	—	102	—	—	—	—	—
Hb. Tal., percentage	80	85	85	85	—	85	—

Days	22	23	24	25	26	27	28
As. parasites	20	—	10,948	11,360	1,600	1,584	1,000
Crescents	160	—	152	20	24	20	8
Maximum temp.	28	30	86	90	54	22	12
Q. bihydrochloride	—	—	—	30	30	*et seq.*	—
Total leucocytes	—	—	62	60	34	33	30
Hb. Tal., percentage	80	—	80	80	75	80	85

Days	29	30	31	32	33	34	35
As. parasites	0	0	0	0	100	0	0
Crescents	8	4	20	24	16	4	4
Maximum temp.	20	20	32	32	20	24	36
Q. bihydrochloride	—	—	—	—	—	—	—
Total leucocytes	—	48	80	130	98	110	85
Hb. Tal., percentage	85	82	82	85	85	85	85

Days	36	37	—	—	—	—	—
As. parasites	—	0	—	—	—	—	—
Crescents	—	0	—	—	—	—	—
Maximum temp.	30	20	—	—	—	—	—
Q. bihydrochloride	—	—	—	—	—	—	—
Total leucocytes	—	65	—	—	—	—	—
Hb. Tal., percentage	—	90	—	—	—	—	—

Case 24.—J. K., steward, 29; Niger; 28 days; April, 126 lbs.

Days	1	2	3	4	5	6	7
As. parasites	5,190	900	1,000	450	900	720	25,000
Crescents	0	0	20	16	88	168	540
Maximum temp.	52	38	26	32	24	52	24
Q. hydrochloride	—	—	—	—	—	—	10
Soamine, grs.	—	—	—	—	—	—	—
Total leucocytes	—	—	—	—	60	80	58
Hb. Tal., percentage	80	80	80	75	72	80	75
Ur. urob., mgs.	—	48	24	11	20	10	0

Days	8	9	10	11	12	13	14
As. parasites	1,000	9,500	3,900	600	—	—	—
Crescents	672	348	548	500	532	564	636
Maximum temp.	80	60	30	36	34	34	32
Q. hydrochloride	—	—	10	—	—	—	—
Soamine, grs.	10	—	8	—	—	8	—
Total leucocytes	36	45	70	50	70	140	160
Hb. Tal., percentage	70	75	75	70	75	80	80
Ur. urob., mgs.	0	—	—	—	—	—	—

Days	15	16	17	18	19	20	21
As. parasites	0	0	200	2,800	1,600	8,300	15,000
Crescents	784	572	520	630	496	367	212
Maximum temp.	24	26	38	40	44	54	54
Q. hydrochloride	—	—	—	—	—	10	30
Soamine, grs.	—	—	5	—	5	—	—
Total leucocytes	75	138	70	45	70	68	60
Hb. Tal., percentage	80	82	82	82	75	75	80
Ur. urob., mgs.	(faecal)	140	—	—	(faecal)	80	—

Days	22	23	24	25	26	27	28
As. parasites	5,600	200	1,000	1,100	0	0	0
Crescents	200	188	132	108	92	128	68
Maximum temp.	54	32	20	34	32	30	24
Q. hydrochloride	30	*et seq.*	—	—	—	—	—
Soamine, grs.	0	0	—	—	—	—	—
Total leucocytes	35	55	42	36	78	56	120
Hb. Tal., percentage	80	82	82	80	82	80	85
Ur. urob., mgs.	—	—	—	—	—	—	—

Case 24—continued

Days	29	30	31	32	33	34	35
As. parasites	—	0	—	0	—	0	—
Crescents	—	28	—	40	—	16	—
Maximum temp.	30	30	24	32	18	22	26
Q. hydrochloride	—	—	—	—	—	—	—
Soamine, grs	—	—	—	—	—	—	—
Total leucocytes	—	90	—	200	—	160	—
Hb. Tal., percentage	—	85	—	85	—	85	—
Ur. urob., mgs.	—	—	—	—	—	—	—
Days	36	37	38	39	—	—	—
As. parasites	0	—	0	0	—	—	—
Crescents	12	—	8	0	—	—	—
Maximum temp.	30	26	22	26	—	—	—
Q. hydrochloride	—	—	—	—	—	—	—
Soamine, grs.	—	—	—	—	—	—	—
Total leucocytes	115	—	200	195	—	—	—
Hb. Tal., percentage	—	—	90	90	—	—	—
Ur. urob., mgs.	—	—	—	—	—	—	—

Case 25.—K. K., sailor, 20; Gambia; 20 days; April, 154 lbs.

Days	1	2	3	4	5	6	7
As. parasites	3,000	4,000	3,956	14,076	13,392	18,000	2,100
Crescents	0	0	0	0	0	0	0
Maximum temp.	86	88	70	98	74	74	28
Q. bihydrochloride	—	—	—	10	20	30	30
Ur. urob., mgs.	76	30	10	—	—	—	—
Faec. urob., mgs.	120	—	—	—	—	—	509
Days	8	9	10	11	12	13	14
As. parasites	2,304	684	2,200	1,120	672	400	0
Crescents	0	0	0	0	0	0	0
Maximum temp.	36	30	32	28	26	26	22
Q. bihydrochloride	*et seq.*	—	—	—	—	—	—
Ur. urob., mgs.	—	—	—	—	—	—	—
Faec. urob., mgs.	—	—	—	—	—	—	—

Case 26.—A. M., sailor, 44; Niger; 20 days; May, 168 lbs.

Days	1	2	3	4	5	6	7
As. parasites	9,700	3,500	2,500	?	?	80	—
Crescents	0	*et seq.*	—	—	—	—	—
Maximum temp.	56	24	14	20	26	24	30
Q. hydrochloride	—	—	—	—	—	—	10
Total leucocytes	66	82	60	90	130	120	124
Hb. Tal., percentage	80	80	80	85	90	90	90
Ur. urob., mgs.	22	18	19	26	15	10	0
Days	8	9	10	11	12	13	14
As. parasites	400	2,000	300	0	0	0	0
Crescents	—	—	—	—	—	—	—
Maximum temp.	22	46	38	24	12	20	34
Q. hydrochloride	30	*et seq.*	—	—	—	—	—
Total leucocytes	160	155	176	168	150	120	—
Hb. Tal., percentage	90	80	88	88	84	90	—
Ur. urob., mgs.	10	—	—	—	—	—	—
Days	15	16	17	18	—	—	—
As. parasites	0	0	—	0	—	—	—
Crescents	—	—	—	—	—	—	—
Maximum temp.	16	10	20	24	—	—	—
Q. hydrochloride	...	—	—	—	—	—	—
Total leucocytes	200	—	178	—	—	—	—
Hb. Tal., percentage	90	—	90	—	—	—	—
Ur. urob., mgs.	—	—	—	—	—	—	—

Case 27.—S. P., trader, 30; W. Africa; Old Blackwater; May, ?

Days	1	2	3	4	5	6	7
As. parasites	1,104	—	—	—	1,056	600	400
Crescents	8	—	—	—	0	4	0
Maximum temp.	—	patient absent			14	12	30
Q. hydrochloride	0	*et seq.*	—	—	—	—	—
Total leucocytes	200	—	—	—	60	120	113
Hb. Tal., percentage	80	—	—	—	70	70	75

Case 28.—J. D., negro fireman, 25 (?); Sierra Leone; Niger; 42 days; June, 151 lbs.

Days	1	2	3	4	5	6	7
As. parasites	3,040	700	40	136	20	—	4
Crescents	0	*et seq.*	—	—	—	—	—
Maximum temp.	24	38	30	32	18	30	24
Q. hydrochloride	—	—	—	—	10	30	30
Total leucocytes	45	30	70	80	80	—	80
Hb. Tal., percentage	—	85	85	90	85	—	90
Ur. urob., mgs.	49	54	0	—	—	—	—
Faec. urob., mgs.	—	1,130	—	—	—	—	—

Days	8	—	—	—	—	—	—
As. parasites	0	—	—	—	—	—	—
Crescents	—	—	—	—	—	—	—
Maximum temp.	24	—	—	—	—	—	—
Q. hydrochloride	20	—	—	—	—	—	—
Total leucocytes	120	—	—	—	—	—	—
Hb. Tal., percentage	90	—	—	—	—	—	—
Ur. urob., mgs.	—	—	—	—	—	—	—
Faec. urob., mgs.	—	—	—	—	—	—	—

Case 29.—M. S., fireman, 38; Niger; 70 days; June, 149 lbs.

Days	1	2	3	4	5	6	7
As. parasites	5,300	6,500	3,800	0	0	0	0
Crescents	0	4	4	0	0	4	0
Maximum temp.	83	69	32	32	32	32	29
Q. hydrochloride	—	20	30	*et seq.*	—	—	—
Pol. leucocytes	21	21	22	15	20	28	41
Mon. leucocytes	12	35	64	18	45	43	100
Hb. Sal., percentage	60	55	65	65	60	60	65

Days	8	9	10	—	—	—	—
As. parasites	0	0	0	—	—	—	—
Crescents	0	0	0	—	—	—	—
Maximum temp.	32	32	25	—	—	—	—
Q. hydrochloride	—	—	—	—	—	—	—
Pol. leucocytes	78	45	20	—	—	—	—
Mon. leucocytes	128	45	30	—	—	—	—
Hb. Sal., percentage	70	65	70	—	—	—	—

Case 30.—J. W., sailor, 53; Niger; 15 days; June, 133 lbs.

Days	1	2	3	4	5	6	7
As. parasites	4,000	2,800	3	8	50	50	12
Crescents	0	0	0	0	0	20	80
Maximum temp.	79	54	22	32	16	18	18
Q. hydrochloride	20	0	*et seq.*	—	—	—	—
Pol. leucocytes	23	22	28	29	22	70	48
Mon. leucocytes	15	85	62	62	30	70	56

Days	8	9	10	11	12	13	14
As. parasites	20	0	0	0	?	0	0
Crescents	120	152	120	116	88	80	72
Maximum temp.	22	22	25	22	29	34	29
Q. hydrochloride	—	—	—	—	—	—	—
Pol. leucocytes	78	35	35	72	42	82	90
Mon. leucocytes	123	60	28	52	50	78	63

Days	15	16	—	—	—	—	—
As. parasites	0	0	—	—	—	—	—
Crescents	68	56	—	—	—	—	—
Maximum temp.	32	25	—	—	—	—	—
Q. hydrochloride	20	20	—	—	—	—	—
Pol. leucocytes	142	63	—	—	—	—	—
Mon. leucocytes	98	73	—	—	—	—	—

Case 31.—J. R., sailor, 20; Niger; 90 days; June, 119 lbs.

Days	1	2	3	4	5	6	7
As. parasites	28,000	14,000	25,600	16,800	3,300	1,200	800
Crescents	0	*et seq.*	—	—	—	—	—
Maximum temp.	95	108	101	87	90	54	61
Methylene blue, grs.	—	4	*et seq.*	—	—	—	—
Pol. leucocytes	15	35	25	18	18	15	15
Mon. leucocytes	5	75	25	24	20	30	30
Hb. Tal., percentage	—	80	85	80	75	80	70

Case 31—*continued*

Days	8	9	10	11	12	—	—
As. parasites	0	0	0	0	0	—	—
Crescents	—	—	—	—	—	—	—
Maximum temp.	29	25	32	29	32	—	—
Methylene blue, grs.	—	—	—	—	—	—	—
Pol. leucocytes	15	17	20	65	92	—	—
Mon. leucocytes	38	39	36	135	88	—	—
Hb. Tal., percentage	65	70	75	75	75	—	—

Case 32.—F. H., sailor, 20; W. Africa; 150 days; July, 150 lbs.

Days	1	2	3	4	5	6	7
As. parasites	60	20	0	0	300	150	200
Crescents	244	100	108	52	80	104	60
Maximum temp.	25	22	25	36	29	40	22
Q. hydrochloride	0	*et seq.*	—	—	—	—	—
Pol. leucocytes	16	28	25	62	60	38	65
Mon. leucocytes...	25	20	62	125	102	48	132

Case 33.—Steward, 18; W. Africa; recently; July, 140 lbs.

Days	1	2	3	4	5	6	—
As. parasites	2,500	6,700	50	—	0	0	—
Crescents	0	*et seq.*	—	—	—	—	—
Maximum temp.	108 delirium	61 delirium	87 delirium	69 delirium	40	32	—
Q. hydrobromide	16	10	10	—	—	—	30 *et seq.*
Pol. leucocytes	55	35	28	—	35	32	—
Mon. leucocytes...	68	40	22	—	52	58	—
Hb. Tal., percentage	105	95	100	—	100	95	—

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